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Letter to the Editor of European Journal of Nuclear Medicine and Molecular Imaging

All that Glitters is not Gold – new reconstruction methods using Deauville criteria for patient reporting

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Abstract

New reconstruction methods can improve lesion detection by improving spatial resolution and reducing image noise. Such methods can result in an increase in lesional uptake, whilst leaving uptake in reference regions such as the mediastinum and liver relatively unaffected. This may alter the interpretation of response assessment in patients with lymphoma using the Deauville criteria. We report how the use of newer reconstruction methods may alter patient management by affecting decisions to de-escalate or escalate treatment using a PET guided approach and urge caution before adopting these newer reconstruction methods in isolation into routine practice.

Dear Sir

We would like to highlight the importance of using EANM Research Ltd (EARL) compliant reconstructions for assessment of lymphoma response using the Deauville criteria [1] in clinical practice.

The recent review in this journal by Aide et al reported that only 38% of EARL accredited centres who responded to a survey, were systematically using EARL compliant reconstructions for quantification [2]. This was despite 88% of these centres being research active.

We recently observed an increase in the number of patients with interim PET 'positive' scans being treated by a regional haematology multidisciplinary team (MDT) for Hodgkin lymphoma in the UK. This coincided with the adoption of Q.Clear (GE) reconstruction [3] for reporting scans at some PET centres.

An independent review of PET-CT scans from eight of these patients with advanced stage disease planned for treatment using a PET response adapted approach [4] was undertaken at the request of the MDT. Baseline and interim scans after 2 cycles of doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) chemotherapy were reviewed using standard ordered subset expectation maximisation (OSEM) VPHD and Q.Clear reconstructions. The interim response scans had been reported as Deauville score 4 for each of the eight patient cases.

For five patient scans, the assessment of the independent reviewer was the same as the local reporter, irrespective of the reconstruction method applied. For two patients, the independent reviewer considered the interim scan to demonstrate a complete metabolic response with Deauville scores of 2 and 3 respectively using OSEM reconstruction. When the Q.Clear reconstruction was applied however, small areas of residual uptake in the right neck in one patient and in a lung mass in the second patient showed increased uptake compared to OSEM reconstruction. This increased uptake using Q.Clear at the site of initial disease was greater than normal liver, i.e. Deauville score 4. One of these patients received escalated treatment, switching from planned AVD chemotherapy to bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisolone (escalated BEACOPP) chemotherapy on the basis of the report.

In a further patient scan, the difference of opinion between reporters was unrelated to the reconstruction but rather to the interpretation of nodal uptake, which was higher than liver using either reconstruction method. The initial reporter considered uptake in a right cervical level II node to represent an involved node, whereas the independent reviewer considered it to be an inflammatory

node, as the node did not demonstrate FDG uptake at baseline and all other sites of baseline disease had resolved.

New image reconstruction methods using resolution or point spread function (PSF) modelling, such as Sharp IR (GE)[5] and HD (Siemens)[6] and Bayesian penalised likelihood techniques, e.g. Q.Clear (GE)[3] represent advances in image reconstruction [7]. These methods improve lesion spatial resolution and reduce noise [8] particularly for small lesions and are more likely to be quantitatively accurate than OSEM [9]. Q.Clear has been reported to lead to improved sensitivity, albeit at the expense of reduced specificity in the detection of malignancy in lung nodules [10], mediastinal nodes in lung cancer [11] and liver metastases from colorectal cancer [12].

However, as uptake in reference 'normal' regions of the mediastinum and liver is largely unaffected [13, 14] the use of these reconstructions can lead to different scoring using the Deauville criteria and interpretation of response assessment for patients with lymphoma using the Lugano Classification [15]. This may alter patient management by affecting decisions to de-escalate or escalate treatment using a PET guided approach, as with the patient reported here. Prospective trials that have validated PET-guided approaches in lymphoma used quality assured data with OSEM reconstruction [4, 16-18].

We urge reporters not to use new reconstruction algorithms in isolation for response assessment [2]. If reporters prefer to use new algorithms for optimal lesion detection, a second dataset with OSEM reconstruction, should be used alongside to provide a Deauville score. We recognise that a single dataset which visually enhances lesion detection, using PSF, but provides similar quantification has been developed (eq.PET, Siemens) [19] which attempts to overcome the requirement to view two image datasets. It may however lead the reporter to select a different 'hottest' residual lesion for quantification purposes compared to OSEM.

Therefore whilst we accept that newer reconstruction techniques may improve diagnosis, we consider that further assessment is required and suggest validation in lymphoma patients before adoption in routine practice. In conclusion, 'All that Glitters is not Gold' and reporters should consider the potential clinical impact of using new reconstruction methods with the Deauville criteria.

Yours faithfully

Sally Barrington

Tom Sulkin

Adam Forbes

Peter Johnson

Compliance with Ethical Standards:

Conflict of Interest: All authors declare they have no conflicts of interest related to this submission.

Ethical approval: This article does not contain any studies with human participants performed by any of the authors.

References

1. Meignan M, Gallamini A, Meignan M, Gallamini A, Haioun C. Report on the First International Workshop on Interim-PET-Scan in Lymphoma. *Leuk Lymphoma* 2009;50:1257-60.
2. Aide N, Lasnon C, Veit-Haibach P, Sera T, Sattler B, Boellaard R. EANM/EARL harmonization strategies in PET quantification: from daily practice to multicentre oncological studies. *European Journal of Nuclear Medicine and Molecular Imaging* 2017;44:17-31.

3. Q.Clear - PET/CT Applications - PET/CT - Molecular Imaging - Nuclear Medicine\PET-CT\PET-Radiopharmacy - Products. Accessed 10/25/2017 2017.
4. Johnson P, Federico M, Fossa A, O'Doherty M, Roberts T, Stevens L, Smith P, Kirkwood A, Sidra G, Trotman J, Berkahn L, d'Amore F, Enblad G, Luminari S, Radford J, Barrington S. Response-adapted Therapy Based on Interim FDG-PET Scans in Advanced Hodgkin Lymphoma First Analysis of the Safety of De-escalation and Efficacy of Escalation in the International RATHL Study (CRUK/07/033). *Hematological oncology* 2015;33:100-80.
5. mi_emea_sharpir_white_paper_pdf_092010_doc0852276.pdf. Accessed 10/25/2017 2017.
6. Panin VY, Kehren F, Michel C, Casey M. Fully 3-D PET reconstruction with system matrix derived from point source measurements. *IEEE Trans Med Imaging* 2006;25:907-21.
7. van der Vos CS, Koopman D, Rijnsdorp S, Arends AJ, Boellaard R, van Dalen JA, Lubberink M, Willemsen ATM, Visser EP. Quantification, improvement, and harmonization of small lesion detection with state-of-the-art PET. *Eur J Nucl Med Mol Imaging* 2017;44:4-16.
8. Alessio AM, Stearns CW, Tong S, Ross SG, Kohlmyer S, Ganin A, Kinahan PE. Application and evaluation of a measured spatially variant system model for PET image reconstruction. *IEEE Trans Med Imaging* 2010;29:938-49.
9. Bettinardi V, Presotto L, Rapisarda E, Picchio M, Gianolli L, Gilardi MC. Physical performance of the new hybrid PETCT Discovery-690. *Med Phys* 2011;38:5394-411.

10. Teoh EJ, McGowan DR, Bradley KM, Belcher E, Black E, Gleeson FV. Novel penalised likelihood reconstruction of PET in the assessment of histologically verified small pulmonary nodules. *Eur Radiol* 2016;26:576-84.
11. Teoh EJ, McGowan DR, Bradley KM, Belcher E, Black E, Moore A, Sykes A, Gleeson FV. 18F-FDG PET/CT assessment of histopathologically confirmed mediastinal lymph nodes in non-small cell lung cancer using a penalised likelihood reconstruction. *Eur Radiol* 2016;26:4098-106.
12. Parvizi N, Franklin JM, McGowan DR, Teoh EJ, Bradley KM, Gleeson FV. Does a novel penalized likelihood reconstruction of 18F-FDG PET-CT improve signal-to-background in colorectal liver metastases?. *Eur J Radiol* 2015;84:1873-8.
13. Kuhnert G, Boellaard R, Sterzer S, Kahraman D, Scheffler M, Wolf J, Dietlein M, Drzezga A, Kobe C. Impact of PET/CT image reconstruction methods and liver uptake normalization strategies on quantitative image analysis. *Eur J Nucl Med Mol Imaging* 2016;43:249-58.
14. Quak E, Le Roux PY, Lasnon C, Robin P, Hofman MS, Bourhis D, Callahan J, Binns DS, Desmonts C, Salaun PY, Hicks RJ, Aide N. Does PET SUV Harmonization Affect PERCIST Response Classification?. *J Nucl Med* 2016;57:1699-706.
15. Cheson BD, Fisher RI, Barrington SF, Cavalli F, Schwartz LH, Zucca E, Lister TA. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol* 2014;32:3059-68.
16. Andre MPE, Girinsky T, Federico M, Reman O, Fortpied C, Gotti M, Casasnovas O, Brice P, van der Maazen R, Re A, Edeline V, Ferme C, van Imhoff G, Merli F, Bouabdallah R, Sebban C, Specht L, Stamatoullas A, Delarue R, Fiaccadori V, Bellei M, Raveloarivahy T, Versari A, Hutchings M, Meignan M,

Raemaekers J. Early Positron Emission Tomography Response-Adapted Treatment in Stage I and II Hodgkin Lymphoma: Final Results of the Randomized EORTC/LYSA/FIL H10 Trial. *J Clin Oncol* 2017;35:1786-94.

17. Engert A, Haverkamp H, Kobe C, Markova J, Renner C, Ho A, Zijlstra J, Kral Z, Fuchs M, Hallek M, Kanz L, Dohner H, Dorken B, Engel N, Topp M, Klutmann S, Amthauer H, Bockisch A, Kluge R, Kratochwil C, Schober O, Greil R, Andreesen R, Kneba M, Pfreundschuh M, Stein H, Eich HT, Muller RP, Dietlein M, Borchmann P, Diehl V. Reduced-intensity chemotherapy and PET-guided radiotherapy in patients with advanced stage Hodgkin's lymphoma (HD15 trial): a randomised, open-label, phase 3 non-inferiority trial. *Lancet* 2012;379:1791-9.

18. Radford J, Illidge T, Counsell N, Hancock B, Pettengell R, Johnson P, Wimperis J, Culligan D, Popova B, Smith P, McMillan A, Brownell A, Kruger A, Lister A, Hoskin P, O'Doherty M, Barrington S. Results of a trial of PET-directed therapy for early-stage Hodgkin's lymphoma. *N Engl J Med* 2015;372:1598-607.

19. EQPET_WP.indd - eq-pet_wp-02580275.pdf. Accessed 11/10/2017 2017.